P-219 - CLASSIC GALACTOSEMIA IN TWO ISOLATED NATIVE POPULATIONS FROM SOUTHERN BRAZIL: PHENOTYPICAL AND GENETIC CHARACTERIZATION

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INTRODUCTION: Classic galactosemia is an inherited condition that can result in complications as hepatocellular damage, failure-to-thrive, developmental delay, cataracts and premature ovarian failure. Diagnosis is established by detection of high levels of galactose-1-phosphate; reduced activity of galactose-1-phosphate uridylytransferase (GALT); and/or by identification of pathogenic variants in GALT gene. It is possible to perform newborn screening (NBS) for this condition, though it is not part of public NBS program in Brazil. Treatment consists on a lactose-restricted diet which is life-saving but cannot prevent long-term complications. Out of the ten individuals with classic galactosemia followed at Hospital de Clínicas de Porto Alegre, four are from two native indigenous populations. OBJECTIVES: To characterize a cohort of patients with Classic Galactosemia from two native populations from Southern Brazil. MATERIALS AND METHODS: Clinical data was obtained through file’s review. DNA was extracted from blood samples. After PCR amplification of individual exons and related intronic boundaries, direct sequence analysis of GALT gene (GenBank NG_009029.1) was performed. RESULTS: Four individuals from three different families were included in the study (male: 3; mean age at inclusion: 6 years). All presented reduced GALT enzyme activity (mean: 2.87 μmol/h/gHb; range: 2-5; NRV: 33-67). They came from isolated populations from Southern Brazil and identified themselves as Native American from two distinct ethnic groups [Guarani (n=1) and Kaingang (n=3)]. Three individuals started symptoms during the first week of life. The mean age of diagnosis was 3.68 years (Range: 0.25-10). Manifestations included developmental delay (3/4); hepatic failure (2/4); feeding problems (2/4); failure-to-thrive (2/4); microcephaly (2/4); extrapyramidal findings (1/4); cataracts (1/4) and cirrhosis (1/4). Besides Classic Galactosemia, one patient also presented with oculocutaneous albinism, deafness and autism, and had normal karyotype. All patients are homozygous for two novel mutations in GALT gene: c.90_91insG (p.His31Alafs*9) and c.529A>G (p.Met177Val). Concerning the second mutation, bioinformatic analyses revealed that it may affect the splicing mechanism, thus being most probably also a pathogenic mutation. CONCLUSION AND DISCUSSION: Our data suggest a higher incidence of Classic Galactosemia among Guarani and Kaingang indigenous peoples from South Brazil is possibly related to endogamy. However, the presence of the same variants in both groups is intriguing.